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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	14

DATE MAILED: 05/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/880,515	COLSTON ET AL.	
	Examiner	Art Unit	
	My-Chau T. Tran	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 36-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 36-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/14/03 has been entered.

2. Applicant's amendment filed 1/14/03 in Paper No. 11 is acknowledged and entered. Claims 1 and 41 are amended by the amendment.

3. Claims 1-9 and 36-43 are pending.

4. Claims 1-9 and 36-43 are treated on the merit in this Office Action.

Withdrawn Rejections

5. All previous rejections for claims 1-9 and 36-43 have been withdrawn in view of applicant's amendments of claims 1 and 41.

New Rejections – Necessitated by Amendment

Claim Objections

6. Claim 41 is objected to because of the following informalities: the term "capture legend" should be replace with "capture ligand". Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-9 and 36-40 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a new matter rejection).

The instant claimed method of claim 1 recites a method for pathogen detection ***composed of sequential operations***. The ***sequential*** method steps comprise:

1) Containing optically encoded microbeads

2) Adding a sample and capture ligand to the contained microbeads

3) Placing the contained microbeads in a mixing holder for sufficient time for the targeted biological sample to adequately bind the microbeads

4) Adding fluorescent labeled antibodies for attachment to the microbead bound sample

5) Attaching the microbeads to a disposable capture substrate containing an array of attachment sites for attaching the microbeads thereto

6) Washing the substrate and attached microbeads

7) Inserting the substrate into an optical detection system for optically decoding the microbeads for identification and measurement of the target biological molecules.

The specification in page 11, paragraph [0038] disclosed the process of the portable detection system. The process comprises the following a method steps:

1) The 'sample is added to a cuvet containing optically encoded microbeads. Each microbead contains a capture ligand a, b, and c, and bioagent-specific antibodies d, e, and f. Each microbead, in addition to the standard sample capture assay, contains special attachment sites.

2) The curvet is then placed in a mixing holder providing time for the targeted biological sample to adequately bind the microbeads.

3) The fluorescent reporter labeled antibodies are added to cuvet that attach to the microbead bound sample.

4) A disposable capture substrate containing a patterned array of attachment sites is inserted into the cuvet. Each attachment site of the array on the disposable capture substrate is designed to capture a single bead with the spatial distance between each site determined by the resolution of the optical detections systems.

5) After the microbeads are attached to the sites of substrate, the substrate is removed from cuvet located in the mixing holder and placed in a wash receptacle.

6) This wash step improves the sensitivity of the detection process by removing from the disposable capture substrate surface all unbound biological constituents and reducing the background solution florescence.

7) Finally, the disposable microbead capture array is placed in a detection shot or reaction chamber where the microbeads are optically decoded for proper identification and measurement of target biological molecules'.

The recitation of *'the method for pathogen detection composed of sequential operations wherein " the first method step" is containing optically encoded microbeads and "the second method step" is adding a sample and capture ligand to the contained microbeads'* claimed in claim 1, have no clear support in the specification and the claims as originally filed. Because specification recites the first method step is that the ***sample is added to a cuvet containing optically encoded microbeads***, does not support the claimed sequential method step of adding a sample and capture ligand to the contained microbeads. Additionally, the first method step of the instant claimed sequential method, which is '*containing optically encoded microbeads*', is contradictory with the subsequence claimed sequential method steps 2-5, because the resulting "product" of these method steps would be the first method step. And from the specification, the microbeads contains 'a capture ligand, bioagent-specific antibodies, and additionally special attachment sites' (page 11, paragraph [0038], lines 3-5). From this description of the microbeads, it is unclear as to what being consider the "optical encoding" of the microbeads. Additionally, the specification disclosed "a portable pathogen detection system wherein ***target biological samples are optically labeled and captured on microbeads***" (pg. 7, paragraph [0020],

lines 1-3; paragraph [0021], lines 2-4). Therefore, an "optically encoded microbeads" is microbeads with target biological samples that are optically labeled.

Further, the specification recites method steps does not support the method steps of the dependent claims as in claims 4, 7-9, and 37-38. For example claim 7, which recites that '*the method of Claim 1, wherein containing the microbeads is carried out by placing the microbeads in a disposable bead pack*'. The first method step recited in the specification is 'sample is added to ***a cuvet*** containing optically encoded microbeads'.

If applicants disagree, applicant should present ***a detailed analysis*** as to why the claimed subject matter has clear support in the specification.

9. Claims 41-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a new matter rejection).

The instant claimed method of claim 41 recites a method for pathogen detection ***composed of sequential operations***. The ***sequential*** method steps comprise:

1) Containing a quantity of microbeads

2) Adding a sample and capture ligand to the contained microbeads

3) Adding fluorescent labeled antibodies for attachment to the microbead bound sample

4) Providing a disposable capture substrate containing an array of attachment sites for attaching the microbeads thereto

5) Inserting the disposable capture substrate containing the array of attachment sites into the contained microbeads for capturing the microbeads

6) Inserting the substrate into an optical detection system for optically decoding the microbeads for identification and measurement of the target biological molecules.

The specification in page 11, paragraph [0038] disclosed the process of the portable detection system. The process comprises the following a method steps:

1) The 'sample is added to a cuvet containing optically encoded microbeads. Each microbead contains a capture ligand a, b, and c, and bioagent-specific antibodies d, e, and f. Each microbead, in addition to the standard sample capture assay, contains special attachment sites.

2) The curvet is then placed in a mixing holder providing time for the targeted biological sample to adequately bind the microbeads.

3) The fluorescent reporter labeled antibodies is added to cuvet that attach to the microbead bound sample.

4) A disposable capture substrate containing a patterned array of attachment sites is inserted into the cuvet. Each attachment site of the array on the disposable capture substrate is designed to capture a single bead with the spatial distance between each site determined by the resolution of the optical detections systems.

5) After the microbeads are attached to the sites of substrate, the substrate is removed from cuvet located in the mixing holder and placed in a wash receptacle.

6) This wash step improves the sensitivity of the detection process by removing from the disposable capture substrate surface all unbound biological constituents and reducing the background solution florescence.

7) Finally, the disposable microbead capture array is placed in a detection shot or reaction chamber where the microbeads are optically decoded for proper identification and measurement of target biological molecules'.

The recitation of *'the method for pathogen detection composed of sequential operations wherein " the first method step" is containing optically encoded microbeads and "the second method step" is adding a sample and capture ligand to the contained microbeads'* claimed in claim 1, have no clear support in the specification and the claims as originally filed. Because specification recites the first method step is that the ***sample is added to a cuvet containing optically encoded microbeads***, does not support the claimed sequential method step of adding a sample and capture ligand to the contained microbeads.

Additionally, the claimed method step 42, which is '*additionally including forming the contained quantity of microbeads to be optically encoded*', is contradictory with the claimed sequential method steps 1-3, because the resulting "product" of these method steps would be the "same" as the "product" of the claimed method step 42.

If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-9 and 36-43 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The method step of "containing optically encoded microbeads" of claim 1 is vague and indefinite. The specification disclosed "a portable pathogen detection system wherein target biological samples are optically labeled and captured on microbeads" (pg. 7, paragraph [0020], lines 1-3; paragraph [0021], lines 2-4). Therefore, an "optically encoded microbeads" is a microbead with target biological samples that are optically labeled. It is confusing that the first step in the ***sequential operations*** is the resulting product of steps 2-4, which are "*adding a sample and capture ligand to the contained microbeads; placing the contained microbeads in a mixing holder for sufficient time for the targeted biological sample to adequately bind the microbeads; adding fluorescent labeled antibodies for attachment to the microbead bound sample*".

b) The term "capture ligand" of claims 1 and 41 is vague and indefinite because it is unclear as to what it is referring to. The specification in page 11, paragraph [0038] and figure 4 disclosed that the microbead contains a capture ligand a, b, and c, and bioagent-specific antibodies d, e, and f. And figure 5 show that it is the bioagent-specific antibody that binds to the sample. Therefore, it is confusing whether the "capture ligand" of claim 1 and 41 compete with the sample to binds to the microbead or it is referring to the "bioagent-specific antibody" on the microbead.

c) There is no antecedent basis for the term "contained microbeads" of claims 1 and 41 in the specification.

d) The method step of "additionally including forming the contained quantity of microbeads to be optically encoded" of claim 42 and the method step of "wherein decoding of the microbeads is carried out in an optical detecting system" of claim 43 are vague and indefinite. Because it is confusing as to how these method step would further limit the sequential method steps of claim 41. For these method steps are the summation of the sequential method steps of claim 41.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-3, 5-6, 36 and 40 are rejected under 35 U.S.C. 102(b) as being anticipate by Pyle et al. (US Patent 5,821,066).

The instant claimed method of claim 1 recites a method for pathogen detection composed of sequential operations. The sequential method steps comprise: 1) containing optically encoded microbeads; 2) adding a sample and capture ligand to the contained microbeads; 3) placing the contained microbeads in a mixing holder for sufficient time for the targeted biological sample to adequately bind the microbeads; 4) adding fluorescent labeled antibodies for attachment to the microbead bound sample; 5) attaching the microbeads to a disposable capture substrate containing an array of attachment sites for attaching the microbeads thereto; 6) washing the substrate and attached microbeads; 7) inserting the substrate into an optical detection system for

optically decoding the microbeads for identification and measurement of the target biological molecules. It is interpreted that steps 2-4 is the method of making the product use in step 1.

Pyle et al. disclose a method for the detection, identification and enumeration of a respiring target bacterium comprising the steps of: a) mixing immunomagnetic beads comprising an antibody (capture ligand) which specifically binds to a target bacteria with a liquid sample comprising said target bacteria; b) allowing said liquid sample to interact with the beads for up to an hour (step a) and b) would refer to step 2) and 3) of the instant claimed method, which would result in step 1) of the instant claimed method); c) placing the sample in a magnetic separator which causes the magnetic beads to which target bacteria have attached to separate from the liquid sample (referring to step 5); d) aspirating the liquid from the liquid sample, leaving the beads with bacteria attached; e) washing the beads with a solution which removes loosely bound bacteria and other particles from the liquid sample (referring to step 6 and claim 6); f) mixing beads with bacteria attached with a fluorochrome dye specific for the detection of respiring bacteria; g) treating bacteria on the beads with a fluorescent stain or a specific fluorescent conjugated antibody (either step f) or g) would refer to step 4)); h) mounting said sample for examination by epifluorescent microscopy, in which a suitable light filter system is used to excite the fluorochrome dye and fluorochrome labeled antibody to fluoresce; and i) quantifying said respiring target bacteria (step h) and i) would refers to step 7 of the presently claimed invention) (col. 12, lines 42-67 to col. 13, line 1). Further, following or simultaneously with incubation with the respiratory indicator, cells on the beads may be treated with a fluorescent stain or a specific fluorescent conjugated antibody (col. 18, lines 2-5). Therefore, either step f) and/or g) would precede step c). The sample is mounted by way of trapping the beads on a filter

membrane and optically read (col. 14, lines 4-20). This would then provide the array pattern on such a membrane (referring to claim 5). The sample suspension containing the beads is allowed to interact for up to an hour, with gentle agitation (col. 17, lines 56-58) (referring to claim 3). Then the method of Pyle et al. anticipates the instant claimed sequential method.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pyle et al. (US Patent 5,821,066) and Nazareth et al. (US Patent 6,319,676 B1).

The instant claimed method of claim 1 recites a method for pathogen detection composed of sequential operations. The sequential method steps comprise: 1) containing a quantity of

microbeads; 2) adding a sample and capture ligand to the contained microbeads; 3) adding fluorescent labeled antibodies for attachment to the microbead bound sample; 4) providing a disposable capture substrate containing an array of attachment sites for attaching the microbeads thereto; 5) inserting the disposable capture substrate containing the array of attachment sites into the contained microbeads for capturing the microbeads; and 6) inserting the substrate into an optical detection system for optically decoding the microbeads for identification and measurement of the target biological molecules. Additionally including the contained quantity of microbeads to be optically encoded (Claim 42). It is interpreted that steps 1-3 is the method of making the product use in the claimed method step 42. Thus, claim 43 is a duplicate of step 6 in claim 41.

Pyle et al. disclose a method for the detection, identification and enumeration of a respiring target bacterium comprising the steps of: a) mixing immunomagnetic beads comprising an antibody (capture ligand) which specifically binds to a target bacteria with a liquid sample comprising said target bacteria; b) allowing said liquid sample to interact with the beads for up to an hour (step a) and b) would refer to step 1) and 2) of the instant claimed method, which would result in step 1) of the instant claimed method); c) placing the sample in a magnetic separator which causes the magnetic beads to which target bacteria have attached to separate from the liquid sample (referring to step 4); d) aspirating the liquid from the liquid sample, leaving the beads with bacteria attached; e) washing the beads with a solution which removes loosely bound bacteria and other particles from the liquid sample; f) mixing beads with bacteria attached with a fluorochrome dye specific for the detection of respiring bacteria; g) treating bacteria on the beads with a fluorescent stain or a specific fluorescent conjugated antibody (either step f) or g) would

refer to step 3)); h) mounting said sample for examination by epifluorescent microscopy, in which a suitable light filter system is used to excite the fluorochrome dye and fluorochrome labeled antibody to fluoresce; and i) quantifying said respiring target bacteria (step h) and i) would refers to step 6 of the presently claimed invention) (col. 12, lines 42-67 to col. 13, line 1). Further, following or simultaneously with incubation with the respiratory indicator, cells on the beads may be treated with a fluorescent stain or a specific fluorescent conjugated antibody (col. 18, lines 2-5). Therefore, either step f) and/or g) would precede step c).

The method of Pyle et al. does not expressly disclose the method step of inserting the disposable capture substrate into the contained microbeads for capturing the microbeads.

Nazareth et al. disclosed a device and method for detecting the presence of analyte in the body fluids (col. 1, lines 44-46). The assay method comprise of a dipstick for dipping in a container of test solution (col. 8, lines 28-30) and a capture site wherein a complex is form comprising immobilized capture agent-capturable conjugate-analyte-labeled binding member (col. 8, lines 45-47).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the method step of inserting the disposable capture substrate into the contained microbeads for capturing the microbeads as taught by Nazareth et al. in the method of Pyle et al. One of ordinary skill in the art would have been motivated to include the method step of inserting the disposable capture substrate into the contained microbeads for capturing the microbeads in the method of Pyle et al. for the advantage of providing an assay system which involves a minimal number of procedural steps, and reproducibility yields reliable results even when used by untrained persons (Nazareth: col. 1, lines 48-50).

Response to Arguments

17. Applicant's arguments with respect to claims 1-9 and 36-43 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 703-305-6999. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 703-306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

mct
May 10, 2003

PADMASHRI PONNAVOLU
PRIMARY EXAMINER